PCT/US2004/009658 WO 2004/087653

WHAT IS CLAIMED IS:

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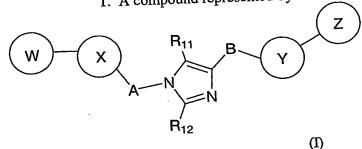
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1. A compound represented by Formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

X and Y each independently is aryl or heteroaryl wherein at least one of X and Y is a heteroaryl with N adjacent to the position of attachment to A or B respectively;

X is optionally substituted with 1-7 independent halogen, -CN, NO_2 , $-C_1$ -6alkyl, $-C_1$ -6alkenyl, $-C_1$ -6alkynyl, $-OR_1$, $-NR_1R_2$, $-C(=NR_1)NR_2R_3$, $-N(=NR_1)NR_2R_3$, $-N(=NR_1)NR_2R_3$, $-NR_1CO_2R_2$, $-NR_1CO_2R_3$, $-NR_1CO_2R_3$, $-SR_4$, $-SO_2R_4$, $-SO_2R_4$, $-SO_2NR_1R_2$, $-COR_1$, $-CO_2R_1$, $-CONR_1R_2$, $-C(=NR_1)R_2$, or $-C(=NOR_1)R_2$ substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to X; wherein the $-C_1$ -6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, $-C_1$ -6alkyl, $-O(C_0$ -6alkyl), $-O(C_3$ -7cycloalkyl), $-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl)($-O(C_0$ -6alkyl))($-O(C_0$ -6alkyl))(-O(C

groups; $R1, R2, \text{ and } R3 \text{ each independently is } -C_{0-6}alkyl, -C_{3-7}cycloalkyl, \text{ heteroaryl, or aryl; any of which is optionally substituted with 1-5 independent halogen, } -CN, -C_{1-6}alkyl, -C_{0-6}alkyl, -C_{0-6}alkyl, -N(C_{0-6}alkyl), -N(C_{0-$

 $R^4 \ is \ -C_1-6alkyl, \ -C_3-7cycloalkyl, \ heteroaryl, \ or \ aryl; \ optionally \ substituted \ with 1-5 \ independent \ halogen, \ -CN, \ -C_1-6alkyl, \ -O(C_0-6alkyl), \ -O(C_3-7cycloalkyl), \ -O(aryl), \ -N(C_0-6alkyl)(C_0-6alkyl), \ -N(C_0-6alkyl)(C_3-7cycloalkyl), \ -N(C_0-6alkyl)(aryl) \ substituents;$

A is $-C_0$ -4alkyl, $-C_0$ -2alkyl-SO- $-C_0$ -2alkyl-, $-C_0$ -2alkyl-SO2- $-C_0$ -2alkyl-NR 9 CO- $-C_0$ -2alkyl-NR 9 CO- $-C_0$ -2alkyl-NR 9 SO2- $-C_0$ -2alkyl- or -heteroC0-4alkyl;

 $Wis-C_{3-7} cycloalkyl, -heteroC_{3-7} cycloalkyl, -C_{0-6} alkylaryl, or -C_{0-6} alkylheteroaryl optionally substituted with 1-7 independent halogen, -CN, NO_{2}, -C_{1-6} alkyl, -C_{1-6} alkynyl, -OR^{1}, -NR^{1}R^{2}, -C(=NR^{1})NR^{2}R^{3}, -N(=NR^{1})NR^{2}R^{3}, -N(=NR^{1})NR^{2}R^{3}$

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 $NR^{1}COR^{2}$, $-NR^{1}CO_{2}R^{2}$, $-NR^{1}SO_{2}R^{4}$, $-NR^{1}CONR^{2}R^{3}$, $-SR^{4}$, $-SO_{2}R^{4}$, $-SO_{2}NR^{1}R^{2}$, $-COR^{1}$, $-CO_{2}R^{1}$, $-CONR^{1}R^{2}$, $-C(=NR^{1})R^{2}$, or $-C(=NOR^{1})R^{2}$ substituents;

Y is optionally substituted with 1-7 independent halogen, -CN, NO₂, -C₁-6alkyl, -C₁-6alkenyl, -C₁-6alkynyl, -OR⁵, -NR⁵R6, -C(=NR⁵)NR⁶R7, -N(=NR⁵)NR⁶R7, -NR⁵COR⁶, -NR⁵CO₂R⁶, -NR⁵CO₂R⁸, -NR⁵CONR⁶R7, -SR⁸, -SOR⁸, -SO₂R⁸, -SO₂NR⁵R⁶, -COR⁵, -CO₂R⁵, -CONR⁵R⁶, -C(=NR⁵)R⁶, or -C(=NOR⁵)R⁶ substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to Y; wherein the -C₁-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, -C₁-6alkyl, -O(C₀-6alkyl), -O(C₃-7cycloalkyl), -O(aryl), -N(C₀-6alkyl)(C₀-6alkyl), -N(C₀-6alkyl)(C₃-7cycloalkyl), or -N(C₀-6alkyl)(aryl) groups;

 R^5 , R^6 , and R^7 each independently is $-C_{0-6}$ alkyl, $-C_{3-7}$ cycloalkyl, heteroaryl, or aryl; any of which is optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$ alkyl, $-C_{0-6}$ alkyl), $-C_{0-6}$

 $R^8 \ is \ -C_1-6alkyl, \ -C_3-7cycloalkyl, \ heteroaryl, \ or \ aryl; \ optionally \ substituted \ with 1-5 \ independent \ halogen, \ -CN, \ -C_1-6alkyl, \ -O(C_0-6alkyl), \ -O(C_3-7cycloalkyl), \ -O(aryl), \ -N(C_0-6alkyl)(C_0-6alkyl), \ -N(C_0-6alkyl)(C_3-7cycloalkyl), \ -N(C_0-6alkyl)(aryl) \ substituents;$

B is $-C_0$ -4alkyl, $-C_0$ -2alkyl-SO- $-C_0$ -2alkyl-, $-C_0$ -2alkyl-SO₂- $-C_0$ -2alkyl-, $-C_0$ -2alkyl-NR¹⁰SO₂- $-C_0$ -2alkyl- or -heteroC₀-4alkyl;

 R^9 and R^{10} each independently is $-C_{0-6}$ alkyl, $-C_{3-7}$ cycloalkyl, heteroaryl, or aryl; any of which is optionally substituted with 1-5 independent halogen, -CN, $-C_{1-6}$ alkyl, $-O(C_{0-6}$ alkyl), $-O(C_{3-7}$ cycloalkyl), -O(aryl), $-N(C_{0-6}$ alkyl)(C_{0-6} alkyl), $-N(C_{0-6}$ alkyl)(C_{3-7} cycloalkyl), $-N(C_{0-6}$ alkyl)(aryl) substituents;

 $Z~is~-C_3-7cycloalkyl,~-heteroC_3-7cycloalkyl,~-C_0-6alkylaryl,~or~-C_0-6alkylheteroaryl~optionally~substituted~with~1-7~independent~halogen,~-CN,~NO_2,~-C_{1-6alkyl},~-C_{1-6alkenyl},~-C_{1-6alkynyl},~-OR^1,~-NR^1R^2,~-C(=NR^1)NR^2R^3,~-N(=NR^$

30 NR 1 COR 2 , -NR 1 CO $_{2}$ R 2 , -NR 1 SO $_{2}$ R 4 , -NR 1 CONR 2 R 3 ,-SR 4 , -SOR 4 , -SO $_{2}$ R 4 , -SO $_{2}$ NR 1 R 2 , -COR 1 , -CO $_{2}$ R 1 , -CONR 1 R 2 , -C(=NR 1)R 2 , or -C(=NOR 1)R 2 substituents;

one of W and Z is optionally absent;

 R^{11} and R^{12} is each independently halogen, $-C_{0-6}$ alkyl, $-C_{0-6}$ alkoxyl, =0, $=N(C_{0-4}$ alkyl), or $-N(C_{0-4}$ alkyl)(C_{0-4} alkyl); and

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any alkyl optionally substituted with 1-5 independent halogen substituents, and any N may be an N-oxide.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

X is 2-pyridyl optionally substituted with 1-4 independent halogen, -CN, NO₂, -C1-6alkyl, -C1-6alkynyl, -OR1, -NR1R2, -C(=NR1)NR2R3, -N(=NR1)NR2R3, -NR1COR2, -NR1CO₂R2, -NR1SO₂R4, -NR1CONR²R3,-SR4, -SOR4, -SO₂R4, -SO₂NR1R², -COR1, -CO₂R1, -CONR¹R², -C(=NR¹)R², or -C(=NOR¹)R² substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to X; wherein the -C1-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, -C1-6alkyl, -O(C0-6alkyl), -O(C3-7cycloalkyl), -O(aryl), -N(C0-6alkyl), -N(C0-6alkyl)(C3-7cycloalkyl), or -N(C0-6alkyl)(aryl) groups.

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3. The compound according to Claim 2, or a pharmaceutically acceptable salt thereof, wherein:

Y is phenyl optionally substituted with 1-5 independent halogen, -CN, NO₂, -C1-6alkyl, -C1-6alkenyl, -C1-6alkynyl, -OR5, -NR5R6, -C(=NR5)NR6R7, -N(=NR5)NR6R7, -NR5COR6, -NR5CO₂R6, -NR5SO₂R8, -NR5CONR6R7, -SR8, -SO₂R8, -SO₂R8, -SO₂NR5R6, -COR5, -CO₂R5, -CONR5R6, -C(=NR5)R6, or -C(=NOR5)R6 substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to Y; wherein the -C1-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, -C1-6alkyl, -O(C0-6alkyl), -O(C3-7cycloalkyl), -O(aryl), -N(C0-6alkyl)(C0-6alkyl), -N(C0-6alkyl)(C3-7cycloalkyl), or -N(C0-6alkyl)(aryl) groups.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

Y is 2-pyridyl optionally substituted with 1-4 independent halogen, -CN, NO₂,
-C1-6alkyl, -C1-6alkenyl, -C1-6alkynyl, -OR⁵, -NR⁵R⁶, -C(=NR⁵)NR⁶R⁷, -N(=NR⁵)NR⁶R⁷, -NR⁵COR⁶, -NR⁵CO₂R⁶, -NR⁵SO₂R⁸, -NR⁵CONR⁶R⁷, -SR⁸, -SOR⁸, -SO₂R⁸, -SO₂NR⁵R⁶,
-COR⁵, -CO₂R⁵, -CONR⁵R⁶, -C(=NR⁵)R⁶, or -C(=NOR⁵)R⁶ substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to Y; wherein the -C1-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further

substituted with 1-5 independent halogen, -CN, $-C_{1-6}$ alkyl, $-O(C_{0-6}$ alkyl), $-O(C_{3-7}$ cycloalkyl), -O(aryl), $-N(C_{0-6}$ alkyl)(C_{0-6} alkyl)

5. The compound according to Claim 4, or a pharmaceutically acceptable salt thereof, wherein:

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X is phenyl optionally substituted with 1-5 independent halogen, –CN, NO₂, -C₁-6alkyl, -C₁-6alkenyl, -C₁-6alkynyl, –OR¹, –NR¹R², –C(=NR¹)NR²R³, -N(=NR¹)NR²R³, – NR¹COR², -NR¹CO₂R², -NR¹SO₂R⁴, –NR¹CONR²R³, –SR⁴, -SO₂R⁴, –SO₂NR¹R², -COR¹, -CO₂R¹, –CONR¹R², -C(=NR¹)R², or -C(=NOR¹)R² substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to X; wherein the –C₁-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, –CN, –C₁-6alkyl, –O(C₀-6alkyl), –O(C₃-7cycloalkyl), –O(aryl), –N(C₀-6alkyl)(C₀-6alkyl), -N(C₀-6alkyl)(C₃-7cycloalkyl), or –N(C₀-6alkyl)(aryl) groups.

6. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

X is phenyl optionally substituted with 1-5 independent halogen, -CN, NO₂, -C₁-6alkyl, -C₁-6alkenyl, -C₁-6alkynyl, -OR⁵, -NR⁵R⁶, -C(=NR⁵)NR⁶R⁷, -N(=NR⁵)NR⁶R⁷, -NR⁵COR⁶, -NR⁵CO₂R⁶, -NR⁵SO₂R⁸, -NR⁵CONR⁶R⁷, -SR⁸, -SOR⁸, -SO₂R⁸, -SO₂NR⁵R⁶, -COR⁵, -CO₂R⁵, -CONR⁵R⁶, -C(=NR⁵)R⁶, or -C(=NOR⁵)R⁶ substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to Y; wherein the -C₁-6alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, -C₁-6alkyl, -O(C₀-6alkyl), -O(C₃-7cycloalkyl), -O(aryl), -N(C₀-6alkyl)(C₀-6alkyl), -N(C₀-6alkyl)(C₃-7cycloalkyl), or -N(C₀-6alkyl)(aryl) groups.

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

Y is phenyl optionally substituted with 1-5 independent halogen, -CN, NO₂, -C1₋6alkyl, -C1₋6alkynyl, -OR⁵, -NR⁵R6, -C(=NR⁵)NR⁶R⁷, -N(=NR⁵)NR⁶R⁷, -N(=NR⁵)NR⁶R⁷, -NR⁵COR⁶, -NR⁵CO₂R⁶, -NR⁵CO₂R⁸, -NR⁵CONR⁶R⁷, -SR⁸, -SO₂R⁸, -SO₂NR⁵R⁶, -COR⁵, -CO₂R⁵, -CONR⁵R⁶, -C(=NR⁵)R⁶, or -C(=NOR⁵)R⁶ substituents, wherein optionally two substituents are combined to form a cycloalkyl or heterocycloalkyl ring fused to Y; wherein

the $-C_{1-6}$ alkyl substituent, cycloalkyl ring, or heterocycloalkyl ring each optionally is further substituted with 1-5 independent halogen, -CN, $-C_{1-6}$ alkyl, $-O(C_{0-6}$ alkyl), $-O(C_{3-7}$ cycloalkyl), -O(aryl), $-N(C_{0-6}$ alkyl), $-N(C_{0-6}$ alkyl), or $-N(C_{0-6}$ alkyl)(aryl) groups.

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- 8. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:
- $Z \ is \ -C_0-6 alkylaryl, \ or \ -C_0-6 alkylheteroaryl \ optionally \ substituted \ with \ 1-7$ independent halogen, -CN, NO₂, -C₁-6 alkyl, -C₁-6 alkenyl, -C₁-6 alkynyl, -OR¹, -NR¹R², 10 C(=NR¹)NR²R³, -N(=NR¹)NR²R³, -NR¹COR², -NR¹CO₂R², -NR¹SO₂R⁴, -NR¹CONR²R³, -SR⁴, -SO₂R⁴, -SO₂NR¹R², -COR¹, -CO₂R¹, -CONR¹R², -C(=NR¹)R², or -C(=NOR¹)R² substituents.
- 9. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein:
 - W is $-C_0$ -6alkylaryl, or $-C_0$ -6alkylheteroaryl optionally substituted with 1-7 independent halogen, -CN, NO_2 , $-C_1$ -6alkyl, $-C_1$ -6alkenyl, $-C_1$ -6alkynyl, $-OR^1$, $-NR^1R^2$, $-C(=NR^1)NR^2R^3$, $-N(=NR^1)NR^2R^3$, $-NR^1COR^2$, $-NR^1CO_2R^2$, $-NR^1SO_2R^4$, $-NR^1CONR^2R^3$, $-SR^4$, $-SO_2R^4$, $-SO_2NR^1R^2$, $-COR^1$, $-CO_2R^1$, $-CONR^1R^2$, $-C(=NR^1)R^2$, or $-C(=NOR^1)R^2$ substituents.
 - 10. The compound according to Claim 3, or a pharmaceutically acceptable salt thereof, wherein:
- $Z is -C_{0-6} alkylaryl, or -C_{0-6} alkylheteroaryl optionally substituted with 1-7 \\ 25 independent halogen, -CN, NO_{2}, -C_{1-6} alkyl, -C_{1-6} alkenyl, -C_{1-6} alkynyl, -OR^{1}, -NR^{1}R^{2}, -C_{1-6} alkyl, -C_{1-6} alkynyl, -OR^{1}, -NR^{1}R^{2}, -C_{1-6} alkynyl, -OR^{1}, -NR^{1}R^{2}, -C_{1-6} alkynyl, -OR^{1}, -NR^{1}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -NR^{1}CO_{2}R^{2}, -C_{1}R^{2}, -C_{1}R^{2},$
- 30 11. The compound according to Claim 5, or a pharmaceutically acceptable salt thereof, wherein:
 - W is $-C_0$ -6alkylaryl, or $-C_0$ -6alkylheteroaryl optionally substituted with 1-7 independent halogen, -CN, NO_2 , $-C_1$ -6alkyl, $-C_1$ -6alkenyl, $-C_1$ -6alkynyl, $-OR^1$, $-NR^1R^2$, $-C_1$ -6alkynyl, $-OR^1$, $-NR^1R^2$, $-C_1$ -1002R3, $-NR^1CO_2R^2$, $-NR^1SO_2R^4$, $-C_1$ -6alkynyl, $-OR^1$, $-OR^1$ -1002R3, $-OR^1$ -102P3, $-OR^1$ -102P3, $-OR^1$ -102P3, $-OR^1$ -102P3, $-OR^1$ -102P3, $-OR^1$

 $NR^{1}CONR^{2}R^{3}$, $-SR^{4}$, $-SO_{2}R^{4}$, $-SO_{2}NR^{1}R^{2}$, $-COR^{1}$, $-CO_{2}R^{1}$, $-CONR^{1}R^{2}$, $-C(=NR^{1})R^{2}$, or $-C(=NOR^{1})R^{2}$ substituents.

12. The compound according to Claim 1, consisting of:

- 5 2-[4-(4-pyridin-3-ylphenyl)-1H-imidazol-1-yl]pyridine;
 - 1-[3-(1-pyridin-2-yl-1H-imidazol-4-yl)phenyl]-1H-pyrrolo[2,3-c]pyridine;
 - 2-[4-(3-pyridin-3-ylphenyl)-1H-imidazol-1-yl]pyridine;
 - 2-[2-fluoro-4-(4-pyridin-2-yl-1H-imidazol-1-yl)phenyl]pyridine;
 - 2-[1-(3-methyl-5-pyridin-3-ylphenyl)-1H-imidazol-4-yl]pyridine;
- 10 3'-methyl-5'-(4-pyridin-2-yl-1H-imidazol-1-yl)-1,1'-biphenyl-2-carbonitrile or a pharmaceutically acceptable salt thereof.
 - 13. The compound according to Claim 1, selected from:

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or a pharmaceutically acceptable salt thereof.

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14. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound according to claim 1, or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

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an opiate agonist, ii) an opiate antagonist, iii) a calcium channel antagonist, iv) a 5HT receptor agonist, v) a 5HT receptor antagonist, vi) a sodium channel antagonist, vii) an NMDA receptor agonist, viii) an NMDA receptor antagonist, ix) a COX-2 selective inhibitor, x) an NK1 antagonist, xi) a non-steroidal anti-inflammatory drug, xii) a GABA-A receptor modulator, xiii) a dopamine agonist, xiv) a dopamine antagonist, xv) a selective serotonin reuptake inhibitor, xvi) a tricyclic antidepressant drug, xvii) a norepinephrine modulator, xviii) L-DOPA, xix) buspirone, xx) a lithium salt, xxi) valproate, xxii) neurontin, xxiii) olanzapine, xxiv) a nicotinic agonist, xxvi) a muscarinic antagonist, xxviii) a selective serotonin and norepinephrine reuptake inhibitor (SSNRI), xxix) a heroin substituting drug, xxx) disulfiram, or xxxi) acamprosate.

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- 16. The pharmaceutical composition according to claim 15, wherein said heroin substituting drug is methadone, levo-alpha-acetylmethadol, buprenorphine or naltrexone.
- 17. The use of the compound of Claim 1 for the preparation of a medicament useful in the treatment of pain disorders, extrapyramidal motor function disorders, anxiety disorders, Parkinson's disease, depression, epilepsy, cognitive disfunction, drug addiction, circadian rhythm and sleep disorders, and obesity.
- 18. The use according to claim 17 wherein said pain disorder is acute pain, persistent pain, chronic pain, inflammatory pain, or neuropathic pain.
- 19. The use of the compound of Claim 1 for the preparation of a medicament useful in the treatment of anxiety, depression, bipolar disorder, psychosis, drug withdrawal, tobacco withdrawal, memory loss, cognitive impairment, dementia, Alzheimer's disease, schizophrenia or panic.
- 20. The use according to claim 17 wherein said disorder of extrapyramidal motor function is Parkinson's disease, progressive supramuscular palsy, Huntington's disease, Gilles de la Tourette syndrome, or tardive dyskinesia.